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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,881	03/28/2002	Akira Matsumoto	082371-000000US	1327

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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 11/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,881	MATSUMOTO, AKIRA	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-7,9,11,16,18-20,24-26,32 and 34-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *3-7, 9, 11, 16, 18, 24-26, 32, and 34-36* is/are allowed.

6)☒ Claim(s) *37-44* is/are rejected.

7)☒ Claim(s) *19 and 20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response, on August 9, 2004, to the Action on the Merits of this case, mailed June 10, 2004, is acknowledged. It is acknowledged that applicants have amended Claims 7, 9, 11, 19, 20, 26, 32, 37, and 38 and added Claims 39-44. Claims 3-7, 9, 11, 16, 18-20, 24-26, 32, and 34-44 are pending and are hereby considered.

Claims-Objections

Claims 19 and 20 are objected to for reciting the same subject matter.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Rejection of Claim 37 under 35 U.S.C. 112, first paragraph, for lack of enablement, as described in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following arguments. That, Claim 37 has been amended to recite a polypeptide consisting of SEQ ID NO: 9 wherein at least 7 residues of SEQ ID NO: 9 are conserved. That, the claimed genus of peptides are useful for the same purpose as SEQ ID NO: 9; in screening for inhibitors of proteolytic function or in a binding assay to reduce an initial pool of candidate compounds to a subset for which inhibitor activity can be determined in an assay using full-length CPB protease. That, "the specification also discloses that antibody against SEQ ID NO:9 inhibits the proteolytic activity human brain CPB (p. 28, lines 34-36), implying that these C-terminal fourteen amino acids occur in the proteolytic domain and are involved in peptidase activity (see also, page 40, lines 2-17). Matslzmoto et al. European J of Neuroscience

1321653-57 (2001); submitted with this response) further confirms the role of this C-terminal sequence in the peptidase activity (see page 1657, left column). Therefore, polypeptides comprising SEQ ID NO:9 are useful for identifying inhibitors of brain CPB protease in screening assays. An initial binding assay (see, e.g., p. 18, lines 15-22) narrows down the number of candidate molecules. A subsequent inhibition assay (and p. 19, lines 18-27) indicates which of the molecules surviving the binding assay actually have proteolytic activity." That, it is not necessary for the skilled artisan to know in advance which amino acids can be modified. Any peptide encompassed by the claim can be used in a binding assay to identify compounds that would bind to the peptide.

It is acknowledged that Claim 37 has been amended. However, these arguments are not found to be persuasive for the following reasons. The specification fails to teach that the peptide of SEQ ID NO: 9 or variants thereof can be used in any assay to test for inhibitors of proteolytic activity or in any assay to test for binding partners. It is acknowledged that the specification at page 28, lines 34-36 discloses that an antibody to the peptide of SEQ ID NO: 9 inhibits the proteolysis of brain APP by the full-length protease. However, a person of ordinary skill in the art would not believe, based on said disclosure, that the said peptide occurs in the proteolytic domain or that any compound that binds to the peptide of SEQ ID NO: 9 would inhibit the protease activity of the full-length protein. Antibodies are very large molecules that can, upon binding, dramatically alter the structure and function of proteins. Small peptides or organic molecules that bind to the motif of SEQ ID NO: 9 are unlikely to have a dramatic effect on the function of the protease unless said motif comprises or controls the catalytic domain. Neither the specification nor the prior art discloses that the peptide of SEQ ID NO: 9 has protease activity or

controls the protease activity of the full-length protein. Moreover, compounds that bind to variants of the peptide of SEQ ID NO: 9 are even less likely to inhibit the activity of the full-length protease.

The specification at page 40, lines 2-17 states the following. "The C-terminal 14 amino acid residues unique to HBCPB have no homology to any portion of the other CPs identified (Figure 4B). The peptide(s) with the highest homology to this sequence is located in the N-terminal adjacent to the light-dependent regulation domain of plant chloroplast ATP synthase γ-subunits from various sources (Figure 4B). ATP synthase catalyzed the synthesis of ATP coupled with an electrochemical gradient of protons produced by the photoelectron transfer chain. Its γ-subunit, which is encoded by the nuclear rather than the chloroplast genome, is believed to be essential in the light-dependent regulation of ATP synthase (Inohara, N. et (1991) J Biol. Chem 266, 7333-7338). The significance of the unique expression of the C-terminal 14 amino-acid peptides (C14) in HBCPB has yet to be clarified, but the homology to the important domain of ATP synthase suggests a relationship with the 265 proteasome is comprised of ATP-dependent proteases and a variety of proteins assembled in association with ATP." The fact that the 14 amino acid peptide of SEQ ID NO: 9 has homology to a region of an ATP synthase would not convince one of skill in the art that the function of said peptide can be deduced from said homology. Neither the specification nor the prior art discloses the function of the region of the ATP synthase that is homologous to SEQ ID NO: 9. Furthmore, the peptide of SEQ ID NO: 9 has a similar level of homology, 53%, to the cation transporter taught by Nakamura et al, 2003 (see enclosed alignment). Thus, a skilled artisan would not know how to use the peptide of SEQ ID NO: 9 based on homology to known proteins.

The prior art reference of Matsumoto et al, 2001 was not submitted with Applicant's response. As a courtesy, the Examiner has acquired said reference for consideration. Matusmoto et al, at page 1657, left column states the following.

> Although peptide library analysis of the C14-module revealed that it is composed of two overlapping epitopes, EP1 and EP2 (Fig. 1), the function of the module and that of each two epitopes remains to be clarified. Recent analysis of proteolysis of the Aβ peptide in a condition with excessive amounts of each oligopeptide has suggested that both the EP1 and EP2 sequences are essential for proper exopeptidase activity for HBCPB (data not shown). This suggests that the C14-module is essential for exopeptidase activity of HBCPB.

Based on the teachings of Matsumoto et al wherein excessive amounts of two fragments of SEQ ID NO: 9 appear to affect cleavage of Aβ peptide, one of skill in the art would not conclude that the motif of SEQ ID NO: 9 comprises or controls the catalytic activity of the full-length protease. Furthermore, the specification fails to assert that the motif of SEQ ID NO: 9 comprises or controls the catalytic activity of the full-length protease. In fact, the specification discloses "The significance of the unique expression of the C-terminal 14 amino-acid peptides (C14) [SEQ ID NO: 9], in HBCPB has yet to be clarified, but the homology to the important domain of ATP synthase suggest a relationship with the 26S proteasome is comprised of ATP-dependent proteases and a variety of proteins assembled in association with ATP" (pg 40, lines 13-17). A person of ordinary skill in the art would clearly not know how to use the peptide of SEQ ID NO: 9, or any variants thereof, based on said disclosure.

Therefore, rejection of Claim 37 under 35 U.S.C. 112, first paragraph, for lack of enablement, is maintained.

Written Description

Rejection of Claim 37 under 35 U.S.C. 112, first paragraph, for insufficient written description, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following arguments. Claim 37 has been amended to recite an isolated peptide consisting of SEQ ID NO: 9 wherein at least 7 amino acid residues are conserved. Said peptides can be used for identifying antibodies useful in detecting brain CPB and inhibitors of brain CPB.

These arguments are not found to be persuasive for the following reasons. Claim 37 is directed to a genus of polypeptides consisting of SEQ ID NO: 9, wherein at least 7 amino acid residues are conserved. The specification does not contain any disclosure of the function of all said polypeptides and does not even assert that said peptides can be used for identifying antibodies useful in detecting brain CPB and inhibitors of brain CPB. The genus of polypeptides that comprise these above protein molecules is a large variable genus with the potentiality of having many different functions, or no function. Therefore, many functionally unrelated peptides are encompassed within the scope of these claims, including partial peptide fragments. The specification discloses the utility of only a single species of the claimed genus, the use of the peptide of SEQ ID NO: 9 to make antibodies, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 37-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described

in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification fails to disclose any polypeptide consisting of SEQ ID NO: 9 wherein at least seven residues of SEQ ID NO: 9 are conserved (as recited in Claims 37, 39, 41, 43), any polypeptide consisting of SEQ ID NO: 9 wherein no more that five residues are replaced deleted, inserted and/or added (as recited in Claims 38 and 40), or any fragment of SEQ ID NO: 9 (as recited in Claims 42 and 44). Therefore, Claims 37-44 are rejected under 35 U.S.C. 112, first paragraph.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Allowable Subject Matter

Claims 3-7, 9, 11, 16, 18, 24-26, 32, and 34-36 are allowable.

Claims 19 and 29 are objected to, but would be allowable if rewritten to address the indicated objections.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sheridan Lee Swope, Ph.D.

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP 1600